REMARKS

Rejection of the Claims Under 35 U.S.C.§112, Second Paragraph

Claims 1 and 2 have been cancelled. Plural forms of different nouns have been rewritten in the singular form, at the suggestion of the Examiner. No narrowing of the claims for any reason related to patentabilty has occurred. Any rejections of the claims under §112, second paragraph should be withdrawn.

Rejection of the Claims Under 35 U.S.C. §112, First Paragraph

Claims 1-8 and 11 stand rejected under §112, first paragraph for allegedly being non-enabled. Applicants respectfully traverse.

Claims 1-7 have been cancelled. Claim 8 has been rewritten to recite a modified recombinant allergen where the dominant T cell-reactive regions of the allergen are not altered by genetic manipulation and wherein at least one, or a combination, of the regions 16-42, 135-149 and 180-206 of the Phl p 5b polypeptide, consisting of a total of 265 amino acids, is/are not altered. One of ordinary skill in the art would readily recognize the structural motifs of the *Gramineae* pollen allergens share high sequence homology. See e.g. the attached alignments which show the sequence homologies for group 5 allergens across various species of *Phleum pratense*. The amino acid sequences are readily obtained from public databases such as Swissprot and EMBL. The sites of the T-cell epitopes and the mutation sites are as indicated on the attachments. Alignment #1 compares the sequences of Phl p 5b, Phl p 5a, Loi p 5a (*Lolium perenne*) and Hol l 5 (*Holcus lantanus*), all of which are grass species. Alignment #2 compares the sequences of Phl p 5a, Phl p 5b, and Phl p 6. Comparison of the different sequences would

readily allow one of ordinary skill in the art to ascertain the respective T-cell epitopes and mutations in the different species. Thus, the arguments of the Examiner which would indicate that undue experimentation would be required to determine which amino acids correspond to which positions e.g., 16-42, 135-149, and 180-206 are without merit and any rejection based thereon should be withdrawn.

Additionally, the applicants have clearly identified the T-cell epitope regions in the recombinant allergens which are important for immunotherapy by using the T-cell clones from patients who are allergic to the *Gramineae* pollen (specification at pages 17-21 and Example 1). Based on the experimental results, applicants could readily ascertain those regions of the recombinant allergen which are important for elliciting reactivity in the T-lymphocytes of allergic patients. The regions in the allergen which may not be altered could be determined. The modified recombinant allergens which meet the requirements of having reactivity with a majority of T_h cells with diminished IgE reactivity possess the requisite properties for being employed as therapeutic agents for allergen-specific immunotherapy (see e.g., specification at page 21-22). Applicants clearly deduced the regions of the allergens which possess the requisite features for making effective mutants of *Gramineae* pollen allergens for immunotherapy. Therefore, any rejection of the claims for lack of enablement or written description should be withdrawn. Further, with respect to the latter, the language of claim 8 and 17 now more clearly describe the minimum structural requirements needed for the invention.

Prior Art

Claims 1-2, and 4-5 have been cancelled and claim 11 has been rewritten to depend from claim 8. Any rejection of these claims under 35 U.S.C. §102 is now considered moot.

Rejections Under 35 U.S.C. §103(a)

Claims 1-6 have been cancelled and claim 11 has been rewritten to depend from claim 8. Any rejection of these claims under 35 U.S.C. §103 is now considered moot and should be withdrawn.

In view of the above remarks and amendments, it submitted that this application is ready for allowance. Early notice to this effect is earnestly solicited. If the Examiner has any remaining issue(s) she is cordially invited to telephone the undersigned at the number given below.

Respectfully submitted,

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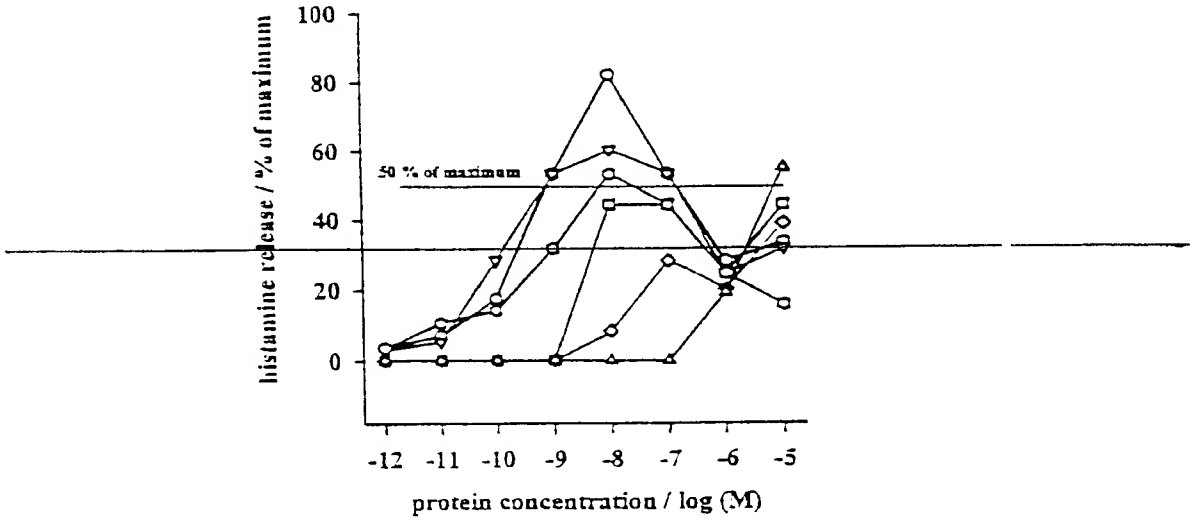
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

On page 48, the first full paragraph has been deleted in its entirety

~~Fig. 6 Release of histamine from human basophils after reaction with the allergens and allergen mutants~~



On page 49, the first full paragraph has been amended as follows:

~~Fig.~~ TABLE 7:

Proliferative reaction of Phl p 5b-reactive T cell clones (TCCs) from allergic patients with rPhl p 5b mutants

On page 50, the first full paragraph has been amended as follows:

~~Fig.~~ TABLE 8:

Proliferative reaction of Phl p 5b-reactive T cell clones (TCCs) from allergic patients with rPhl p 5b mutants

On page 51, the first full paragraph has been amended as follows:

~~Fig.~~ TABLE 9:

Proliferative reaction of Phl p 5b-reactive T cell clones (TCCs) from allergic patients with rPhl p 5b mutants

On page 53, the first full paragraph has been amended as follows:

~~Fig.~~ TABLE 10:

Proliferative reaction of the Phl p 5b-reactive T cell lines (TCLs) from allergic patients with rPhl p 5b mutants

IN THE CLAIMS:

Please **amend** the claims as follows:

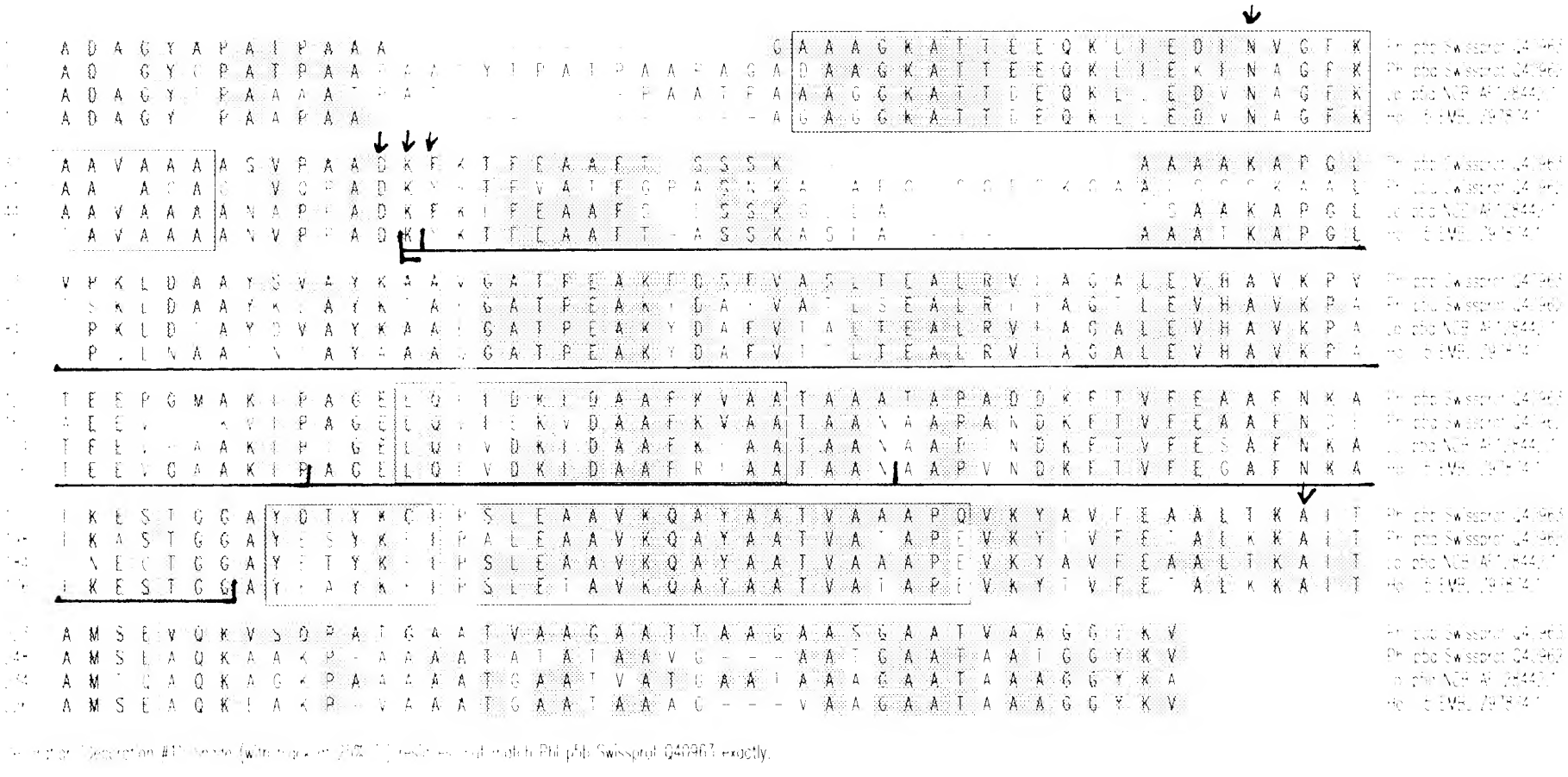
8. (Amended) A modified ~~Modified~~ recombinant ~~allergens according to claim 5~~ allergen wherein ~~characterized in that~~ at least one~~, or a combination,~~ of the T-cell reactive regions 16-42, 135-149 and 180-206 of the Phl p 5b polypeptide, consisting of a total of 265 amino acids, is/~~are~~ not altered.

9. (Amended) A ~~Modified~~ modified recombinant ~~allergens~~ allergen according to claim 8, selected from ~~the following group of polypeptides :~~

PM1	(N^{32} → D, D^{49} → L, K^{50} → A)	(SEQ ID NO. 88)
PM2	(D^{49} → L, K^{50} → A)	(SEQ ID NO. 89)
PM3	(A^{13} → C)	(SEQ ID NO. 90)
DM1	(Δ K^{50} → $P^{\Delta 132}$, D^{49} → L)	(SEQ ID NO. 91)
DM2	(Δ F^{51} - G^{178}, D^{49} - L, K^{50} - A)	(SEQ ID NO. 92)
DM2*	(Δ F^{51} - G^{178}, 179 - 217 altered sequence) or	
DM3	(Δ A^{154} - T^{177}, A^{220} → T)	(SEQ ID NO. 93)

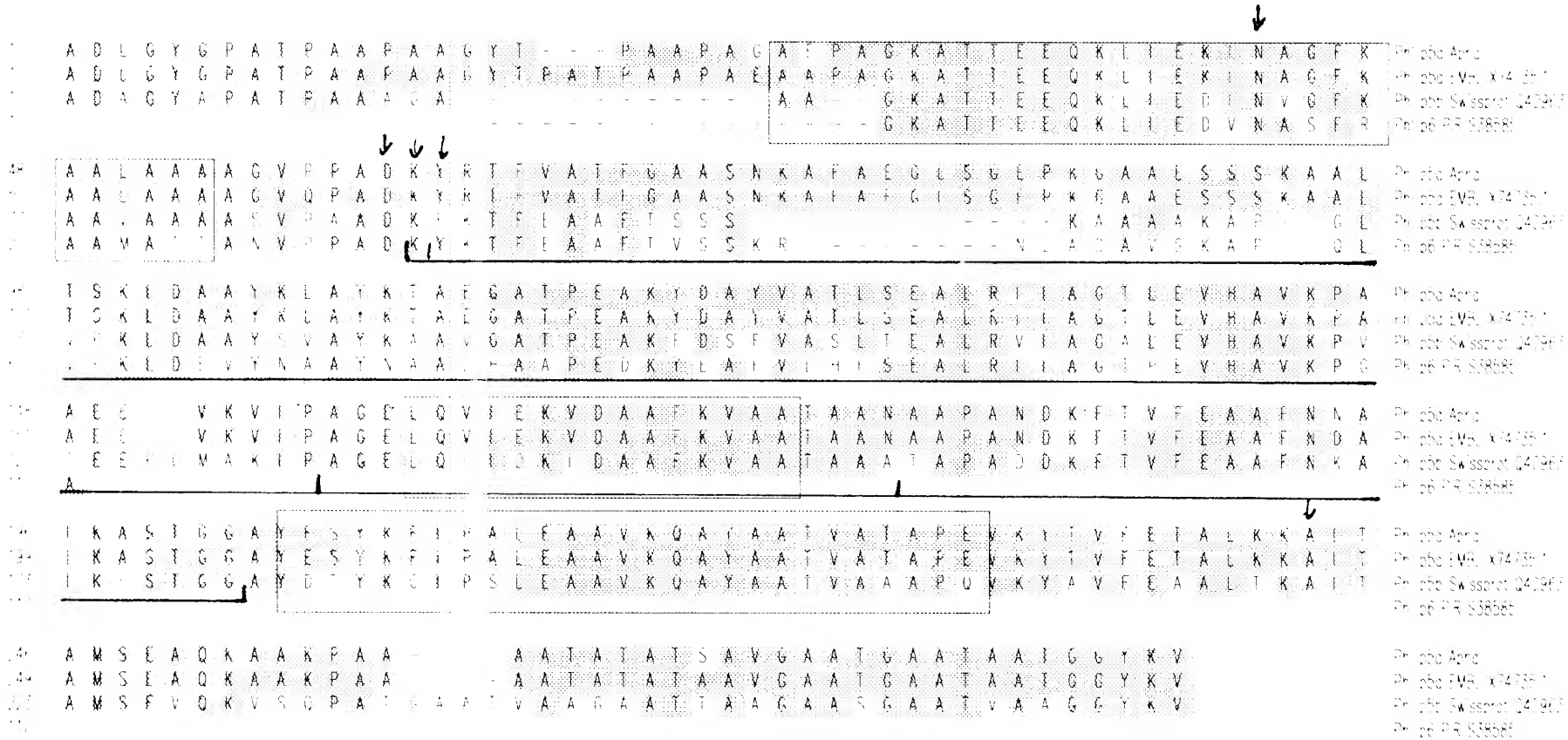
11. (Amended) A ~~Pharmaceutical~~ pharmaceutical preparation for treating an IgE-mediated allergy comprising ~~one or more~~ at least one modified recombinant ~~allergens~~ allergen according to claim ~~1~~ 8 ~~and/or one of their physiologically harmless salts or solvates and also, where appropriate, additional active compounds and/or auxiliary substances, for treating IgE-mediated allergies~~ and a pharmaceutically acceptable carrier.

Alignment Report of *Phleum pratense* 5a-und 5b and group 5 of *Lolium perenne* and *Holcus lanatus*



Legend: ↓ point mutation sites | all mutants except for PM3
— deletion sites
green boxed: T-cell epitopes of Phl p5b (aa 16-42, 136-150, 181-207)

Alignment Report of *Phleum pratense* 5a und b-Variants and Phl p6



Legend: ↓ point mutation sites ⎫ all mutants except for PM3
—— deletion sites ⎭
green boxed: T-cell epitopes of Phl p5b (aa 16-42, 136-150, 181-207)